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EXAMINER

CLOW, LORI A

ART UNIT

PAPER NUMBER

1631

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/004,587

Applicant(s)

TAINSKY ET AL.

Examiner

Lori A. Clow, Ph.D.

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 19 July 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 20 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

Applicants' Supplemental response, filed 19 July 2007, has been fully considered.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim 20 is currently pending. Claims 1-19 have been cancelled.

#### **Claim Rejections - 35 USC § 112**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. *This rejection is necessitated by amendment.*

Claim 20 recites, "a method of detecting and identifying markers indicative of early stage cancer" in the preamble. The final step of the claim recites, "including all epitopes identified in protein array assays for detecting early stage cancer". The claim is unclear because there is no positive, active method step of detecting or identifying any marker that is indicative of early stage cancer. Are the epitopes supposed to be the markers, for instance? Clarification is requested.

Claim 20 recites, "differentially biopanning sera obtained from a normal individual and patients with cancer against phage display libraries". The preamble states that the method is for

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detecting “early stage cancer”. The claims is unclear because is the patients are already known to have cancer, then what is indicative of early stage cancer? Clarification is requested.

Claim 20 recites, “including all epitopes identified in protein array assays for detecting early stage cancer”. It is unclear what Applicant intends as the claim limitation of this step. The claim appears to read “including all epitopes identified in protein array assays”. However, no protein array assays were performed in previous steps”. Perhaps Applicant intends that the claim read, “including all identified epitopes in a protein array assay designed to detect early stage cancer” or something similar. Clarification is requested.

#### **Claim Rejections - 35 USC § 102**

Claim 20 is rejected under 35 U.S.C. 103(b) as being unpatentable over Sioud et al. (European Journal of Immunology (2001) Vol. 31, pages 716-725; recited previously). ***This is necessitated by amendment.***

The instant claims are drawn to a method of detecting and identifying markers indicative of early stages of cancer by biopanning sera from a normal individual patients and patients with cancer, identifying epitope bearing clones displaying reactivity to antibodies present in sera of patients with early stage cancer but not in sera of normal individuals, identifying all epitope bearing clones specific to early stage cancer and including all epitopes in protein array assays.

In regard to claim 20, Sioud teaches the analysis of the humoral response in patients with cancer. Libraries from breast cancer cell lines were biopanned and positive clones were selected. Using serum antibodies from patients with breast cancer, IgG-binding phage-encoded cDNA products were selected and the clones identified important antigens including p53, pentraxin and

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others. The selected phage-displayed cDNA products were recognized by a significant number of breast cancer sera as compared to normal individuals (abstract; Results and Discussion section 2.2 on page 717).

A computer is utilized to quantitate densitometric imaging on an immunospot assay that was used to determine the presence or absence of antibodies against the selected phage-encoded cDNA products in normal and cancer patient sera. Thus, “identifying” results of the biopanning step (page 718, column 1, paragraph 1).

Sioud et al. includes the following at page 717, columns 1 and 2 in reference to protein arrays:

As the first step towards an extension of the phage display technology to the construction and screening of complex repertoires representing genes expressed by a given cell population, oligo (dT)-primed cDNA repertoires from T47D and MCF-7 breast cancer cell lines were cloned into the phagemid vectors pG6A, pG6B and pG6C. The system is based on the covalent linkage of cDNA-encoded products to the C terminus of the M13 coat protein VI in all three reading frames [26]. The suitability of the pG6 libraries, designated oligo (dT) library (dTL), was first investigated by biopanning on rabbit polyclonal IgG directed against the human Bcl-protein. After five rounds of selective enrichment, positive clones were identified by immunoscreening (Fig. 1A). Lysates from a positive phage displaying the Bcl-XL gene product, determined by DNA sequencing, and from a control phage were **analyzed by a Western blot** (Fig. 1 B). A band corresponding to the pVI-Bcl-xL fusion protein was identified by the anti-human Bcl-XL IgG (lane 2). No reactivity was seen with the wild-type phage lysate (lane 1). These data confirm the utility of the pVI expression system as suggested by Jespers et al. [26]. Positive clones were also detected after the third round of selection (data not shown).

It is clear that Sioud et al. teach all embodiments of the instantly *claimed* invention.

***Response to Applicant's arguments:***

1. As the rejection has been changed from obviousness to anticipation, Applicant's arguments are moot with regard to the “microarray”, as it is no longer recited in the claims as

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amended. Therefore, the claims read on **any** protein array and Sioud et al. teaches such limitations.

2. With regard to Sioud et al., Applicant argues the following:

a. There is no suggestion or disclosure in the Sioud et al. reference of a method or assay that simultaneously screens for an unlimited number of markers within sera.

This is not persuasive. Sioud et al. teaches the identification of markers in patients with cancer versus normal individuals, as indicated above. Sioud et al. do identify more than one marker, as also indicated above, from panned sera. In addition, the claimed invention does not require that the method (the assay is not claimed) simultaneously screen an unlimited number of markers within sera. The inclusion of all epitopes that were identified in cancer versus non-cancer individuals was performed by Sioud et al. on page 718, for example:

Positive phage clones are clearly distinguishable from negative clones, confirming the specificity of the immunoreaction. To evaluate the presence or absence of antibodies against the selected phage-encoded cDNA products in normal and cancer patient sera, phage particles from random individual positive clones were purified and tested by an immunospot assay (Fig. 3) as a representative example. The immunoreactivity was quantitated with densitometric imaging using ImageQuant software. Most phages showed a strong reactivity with patient IgG as compared to the reactivity obtained with normal IgG.

b. Applicant argues that the invention is “high throughput” and that is not taught by Sioud et al.

This is not persuasive, as the method as now claimed, is not directed to or limited to be a high throughput method.

c. Applicant argues that the goal of the Sioud et al. reference is to “enrich for the best binders” and therefore teaches away from a large array.

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This is not persuasive. Firstly, the claimed method is not limited to a large array and therefore, this argument is moot. Secondly, while the goal of Sioud et al. may be to enrich for the best binders, Sioud et al. does not preclude finding multiple markers, as indicated in the previous Office Action and above. Furthermore, Applicant admits that Sioud et al. teach biopanning libraries to select phage display cDNA products recognized by a significant number of breast cancer sera as compared to normal individuals, which is what is now claimed in instant claim 20.

d. Applicant argues that the present invention provides unexpected results as it is characterized by identifying all epitope-bearing clones that are specific to early-stage cancer.

This is not persuasive, as Sioud et al. have provided the exact same results; therefore the results are not unexpected.

e. Finally, Applicant argues that the prior art does not provide markers nor does it suggest the provision of markers for such early stage cancer detection. Applicant states that treatment of early-stage cancer is known to be significantly more effective than treatment of later-stage cancer.

This is not persuasive. The claimed preamble states that the invention is for “detecting and identifying markers of early stage cancer”. However, sera are biopanned from patients with cancer (therefore the patients have already been identified as *having* cancer) versus normal individuals. Sioud et al. teach the exact method of biopanning patients with cancer and normal individuals. Therefore, the claimed method does not distinguish over the prior art. Lastly, the claimed method is not directed to, nor does it claim, a method of treatment. Therefore this argument is moot.

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### **Conclusion**

No claims are allowed.

The outstanding rejections under 25 USC 103 have been withdrawn in view of the amendments to the claims. However, may be re-instated if further amendments are applied.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### **Inquiries**

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735.



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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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July 31, 2007

Lori A. Clow, Ph.D.

Primary Patent Examiner

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LORI A. CLOW, PH.D.  
PRIMARY EXAMINER

